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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/715,902	11/17/2000	John James Donnelly	1627.003	5612

27476 7590 01/21/2005

Chiron Corporation  
Intellectual Property - R440  
P.O. Box 8097  
Emeryville, CA 94662-8097

EXAMINER
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WEHBE, ANNE MARIE SABRINA

ART UNIT	PAPER NUMBER
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1632

DATE MAILED: 01/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

**Advisory Action**

Applicati n N .

09/715,902

Applicant(s)

DONNELLY ET AL.

Examin r

Anne Marie S. Wehbe

Art Unit

1632

--The MAILING DATE of this communicati n appears on the cover sheet with the corres ndenc address --

THE REPLY FILED 14 December 2004 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

**PERIOD FOR REPLY [check either a) or b)]**

- a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.
- b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on \_\_\_\_\_. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.
2. ☐ The proposed amendment(s) will not be entered because:
- (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);
  - (b) ☐ they raise the issue of new matter (see Note below);
  - (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
  - (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: \_\_\_\_\_

3. ☐ Applicant's reply has overcome the following rejection(s): \_\_\_\_\_.
4. ☐ Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
5. ☒ The a) ☐ affidavit, b) ☐ exhibit, or c) ☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: see attached.
6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.
7. ☐ For purposes of Appeal, the proposed amendment(s) a) ☐ will not be entered or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: \_\_\_\_\_.

Claim(s) objected to: \_\_\_\_\_.

Claim(s) rejected: \_\_\_\_\_.

Claim(s) withdrawn from consideration: \_\_\_\_\_.

8. ☐ The drawing correction filed on \_\_\_\_\_ is a) ☐ approved or b) ☐ disapproved by the Examiner.
9. ☐ Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s). \_\_\_\_\_.
10. ☐ Other: \_\_\_\_\_

**Attachment to Advisory Action**

**5. cont.** Applicant's arguments have been considered but have not been found persuasive in overcoming the rejection of all pending claims under 35 U.S.C. 103(a) over Song et al., Hedley et al., and Fattal et al. The rejection of record stands. The applicant argues that the particles taught by Fattal et al. are nanoparticles, not microparticles as claimed, or as taught in Hedley. In response, please note that the claims as written encompass the same size particles as taught by Fattal et al., see for example claim 30 which depends on independent claim 1 and recites that the microparticles have diameters ranging from "about 500 nm to about 30  $\mu$ m". Fattal et al. teaches particles which are about 500nm in diameter. Further, please note that the compositions of microparticles taught by Hedley et al. include particles of about 500nm as well, see for example Figure 2 of Hedley et al. The applicant further argues that because of the size difference in the particles taught by Hedley et al. and those of Fattal et al., the Fattal et al. particles would not be phagocytosed, and thus there would be no motivation to combine the teachings of Fattal et al. with Hedley et al. In response, the art, including the art provided by applicants, teaches that cells use several different methods to uptake foreign matter, including phagocytosis and endocytosis. The claims as written do not include any limitation as to the mechanism by which the microparticles enter the dendritic cells. At the time of filing, particles of many different sizes were known to be successfully taken up by cells. In fact, both Hedley et al. and Fattal et al. demonstrate success uptake of particles of different sizes comprising nucleic acids by cells. Thus, the art of record shows that both particles less than 1  $\mu$ m and particles greater than 1  $\mu$ m can successfully deliver nucleic acids into cells. Further, please note that Fattal et al. does in fact teach that the nanoparticles are taken up by cells via an endocytic/phagocytic pathway (Fattal et al., page 137, abstract). In addition, and as stated in the previous office actions, Fattal et al. provides motivation to include cationic detergent in particles for nucleic acid delivery by teaching that the inclusion of cationic detergent increases the amount of polynucleotide associated with the particles and increases the cellular uptake of these particles by cells. Finally, the applicant argues that since Fattal et al. teaches the delivery of oligonucleotides, not expression vectors, there is no reasonable expectation of success that vectors introduced using the methods of Fattal et al. would in fact be expressed. In response, the previous office action

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discussed the fact that the prior art demonstrates that many different methods are useful for introducing expression vectors into cells. The art further demonstrates that once in the cell, the vector expresses any encoded gene which is operably linked to appropriate expression elements. Both Song et al. and Hedley et al. provide specific examples of gene expression after the uptake of expression vectors via different routes such as introduction by viruses, liposomes, and microparticles. As a result, the skilled artisan would reasonably expect that successful delivery of an expression vector into a cell would be followed by gene expression. Since Fattal et al. demonstrates the successful delivery of nucleic acid into cells using particles containing cationic detergents, the skilled artisan would therefore have had a reasonable expectation of success that delivery of expressible nucleic acids using the same technique would in fact result in gene expression.

Any inquiry concerning this communication from the examiner should be directed to Anne Marie S. Wehbé, Ph.D., whose telephone number is (571) 272-0737. The examiner can be reached Monday- Friday from 9:30-6:00 EST. If the examiner is not available, the examiner's supervisor, Amy Nelson, can be reached at (571) 272-0804. For all official communications, **the new technology center fax number is (571) 273-8300**. For informal, non-official communications only, the examiner's direct fax number is (571) 273-0737.

Dr. A.M.S. Wehbé

ANNE M. WEHBE' PH.D  
PRIMARY EXAMINER

